



PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 20627WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/NL 03/00262	International filing date (day/month/year) 07.04.2003	Priority date (day/month/year) 09.04.2002
International Patent Classification (IPC) or both national classification and IPC C07C213/08		
Applicant DSM N.V. et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
- I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand 03.11.2003	Date of completion of this report 07.09.2004
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer O'Sullivan, P Telephone No. +31 70 340-4511 

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International application No. PCT/NL 03/00262

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-11 as originally filed

Claims, Numbers

1-9 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

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**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-9
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-9
Industrial applicability (IA)	Yes: Claims	1-9
	No: Claims	

2. Citations and explanations

see separate sheet

Re: Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The following documents (D) are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

- D1: Beilstein [online] reaction ID 246889 (XP2214315)
D2: Beilstein [online] reaction ID 1841461 (XP2214308)
D3: Matthews, B R in Tetrahedron Letters, Vol 30, No 38, pp 5157-5158

1. Novelty (Art 33(2) PCT)

The process of the current application concerns the production of enantiomerically enriched α -amino aldehydes, aldehyde derivatives or β -amino alcohols from their corresponding nitriles by hydrogenation in the presence of hydrogen, a hydrogenation catalyst and a mineral acid. None of the prior art discloses this reaction with an enantiomerically enriched carbon in the C* position, therefore the subject-matter of claims 1-9 is considered new.

2. Inventive Step (Art 33(2) PCT)

D1 may be considered as the closest prior art since it discloses the same reaction as the current application (Hydrogenation of nitrile with H₂/ Pd in the presence of a mineral acid to yield an alcohol) for compounds falling under the scope of claim 1 with the exception that the compounds do not contain an asymmetric C* carbon atom. The difference between the current application and D1 is the asymmetric carbon, C*. The effect of this difference is the ability to produce alcohols containing an asymmetric carbon by hydrogenation of nitriles containing an asymmetric carbon in position C*. Therefore the problem underlying the current application may be formulated as how to transform asymmetric amino nitriles into the corresponding alcohols/aldehydes without epimerization of the asymmetric centre. The solution is to use the known hydrogenation process disclosed in D1. The solution to this problem is considered obvious for the following reasons:

The skilled man is aware from the prior art that amino nitriles can be transformed into either alcohols or aldehydes by hydrogenation in the presence of a catalyst and a mineral acid. The reaction proceeds *via* hydrogenation to the imine/amine followed by hydrolysis to the aldehyde/alcohol. The skilled man knows that the C-C* bond (where C is the nitrile carbon and C* the asymmetric carbon) is not broken during the reaction

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and therefore no change in the symmetry around C* would be expected. Would this not be apparent to the skilled man, he would use his knowledge of D3 in which the H₂/Ni hydrogenation of a *β*-hydroxy nitrile proceeded with retention of stereochemistry at C* to lead him to the solution proposed in the current process.

The subject-matter of claims 1-9 is therefore not considered to fulfill the requirements of Art 56 EPC.